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Occipital Encephalocele and MURCS Association: Case Report and Review of Central Nervous System Anomalies in MURCS Patients

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The combination of MURCS association (Müllerian duct and renal agenesis, upper limb and rib anomalies) and occipital encephalocele occurred in a stillborn girl of 41 weeks gestation. The malformations are compatible with a defect in the organization of the paraxial mesoderm that gives rise to occipital, cervical, and thoracic somites and adjoining intermediate mesoderm. These structures contribute to the occipital bone, cervical spine, upper limbs, and urogenital system. Brain imaging may be useful in assessing MURCS patients, if cranial malformations prove to be clinically important in these individuals. © 1996 Wiley-Liss, Inc.

KEY WORDS: encephalocele, MURCS association, paraxial mesoderm

INTRODUCTION

Occipital encephaloceles are developmental anomalies of the skull and neural tube [Ingraham and Swan, 1943]. MURCS association consists of Müllerian duct (MU), renal (R), and cervicothoracic somite (CS) malformations [Duncan et al., 1979]. We describe a stillborn girl who had an occipital encephalocele and MURCS association. The case adds to the list of MURCS manifestations and supports a paraxial mesoderm mechanism for embryogenesis of encephaloceles and MURCS.

CLINICAL HISTORY

A stillborn female was delivered spontaneously following a 41-week pregnancy to a 25-year-old gravida 4, para 3 Mexican mother. The father was 42 years old. The mother had had prenatal care and denied use of tobacco, alcohol, or drugs. Ultrasound examination at 28 weeks showed severe oligohydramnios, a large encephalocele, and bilateral renal agenesis. One brother and 2 sisters (ages 3, 2, and 1, respectively) were healthy. Both paternal grandparents were from a pueblo (3,000 inhabitants) in Michoacan, Mexico, and the maternal grandmother was from the same area. There was no known consanguinity, and none of the 4 grandparents had the same family name.

CLINICAL AND AUTOPSY FINDINGS

The weight was 1,340 g, crown-heel length 40 cm, crown-rump length 29 cm, and OFC 25 cm (all <5th centile). A skin-covered, fluid-filled, occipital encephalocele was present (Fig. 1). There was a 0.5–1 cm round skin defect at the vertex of the cranium. Palpebral fissures were 1.5 cm (normal for age), and the inner canthal distance was 1.5 cm (3rd centile). Irides were normal. Ears were 3.3 cm (3rd–25th centile), had soft, overfolded helices, and were not low-set. The nose looked as if it had been pushed downward. The lip and palate were not cleft. The mandible was small, and the neck was short and webbed. The right thumb was absent. The right hand was 4.0 cm, and the palm was 2.3 cm (both <3rd centile). The left hand (4.5 cm with a palm of 3.0 cm, both 3rd centile) had a single palmar crease. There was no poly- or syndactyly. The left elbow extended to 90 degrees. The chest (internipple distance 5 cm, <3rd centile) and back appeared normal. Hips were flexed to 90–120 degrees, and there was valgus deformity of both feet. Feet were 6 cm.

The thymus (1 g; reference 4 ± 2 g), lungs (combined 9 g; reference 27 ± 7 g), and liver (30 g; reference 60 ± 16 g) were hypoplastic. Both kidneys were absent. The bladder was small with an empty lumen. The right ovary was not identified, and a streak ovary attached to a fibrous cord was found on the left. Fallopian tubes and uterus were absent. Vagina, clitoris, and labia were normal, except the vagina appeared to end in a blind sac. The remaining visceral organs were normal in structure and weight. The umbilical cord was normal with 3 vessels. The anus was patent and passed meconium stool. Findings are summarized in Table I.

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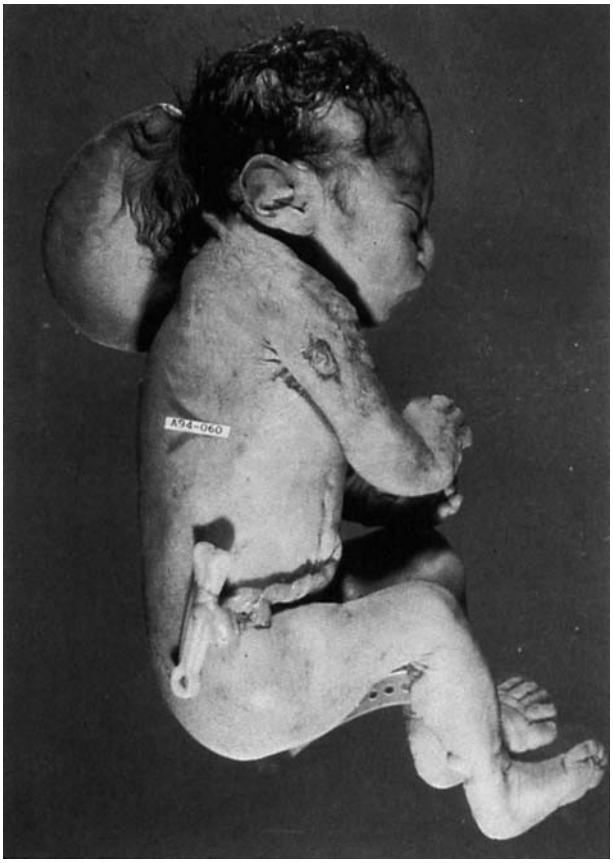

Fig. 1. The stillborn girl with an occipital encephalocele.

Karyotyping showed a 46,XX chromosome constitution.

The 200 g brain was attached to an 8 × 4 cm, midline, occipital encephalocele. The dura appeared normal. The frontal suture was completely fused, with no anterior fontanelle. The cranial bones were of usual thickness and unremarkable in shape, except the occipital bones were somewhat small. The frontal and parietal lobes were covered with thin, transparent meninges and were tan with parasagittal gyral grooves and small surface veins. The left cerebellum and posterior left occipital lobe were connected by a membranous pedicle, which extended to the encephalocele through a triangular, occipital bregma suture defect (1.5 cm). The exterior portion of the encephalocele was covered anteriorly by a shiny, dark red, vascular arachnoid membrane and posteriorly by skin with black hair. No brain tissue was grossly seen in the encephalocele, which contained concentric membranous lamellae. Shallow polymicrogyral formation was evident in the left hemisphere and, to a lesser degree, in the right cerebral hemisphere. The cerebellum, pons, and midbrain were small. The left cerebellar hemisphere was half the size of the right, with gross malformation of the vermis and folial pattern of the hemispheres. There was no Arnold-Chiari malformation.

Coronal sections of the brain showed a vestigial fornix and a very narrow corpus callosum (3 mm). The gyri were shallow and irregular over both cerebral hemispheres with a thick-appearing gray strip and no evidence of cerebral myelination. The anterior lateral ventricles were symmetrical and not enlarged. Architecture of the basal ganglia, thalamus, and hypothalamus was unremarkable. The lateral ventricles were enlarged posteriorly with communication by probe through the encephalocele pedicle from the left side.

Sections of the cerebellum showed left-sided folial displacement and reduction of numbers compared to the right side. However, the cellular architecture of the folia was near normal.

Microscopic sections of the encephalocele cyst showed that a portion of the left cerebellum had herniated into

TABLE I. MURCS Association With Central Nervous System Malformations

	Case 1[a]	Case 2[b]	Current case
Brain	cerebellar cyst; cortical heterotopia	NR	occipital encephalocele
Spinal cord	NR[c]	thoracolumbar meningomyelocele	normal
Skull	NR	NR	small occipital bones; occipital suture defect; lückenschädel
Spine	incomplete C6; fusion of T2-T3	cervicothoracic hemivertebrae; cervical fusions	no abnormality seen by X-ray
Upper limbs	NR	NR	bilateral Sprengel deformity; right radial hypoplasia and absent thumb
Ribs	supernumerary C7 and L1 ribs	absent right 1st and 3rd; fused right 4th and 5th	11 pairs; fused T2, T3, and T4
Kidneys	single right	single left, dysplastic	bilateral agenesis
Ureters	single right	single left, stenotic	absent
Bladder	agenesis of left trigone	NR	small
Ovaries	NR	elongated; normal histology	single left; streak
Oviducts	absent	rudimentary	absent
Uterus	small buds of smooth muscle	absent	absent
Vagina	agenesis of proximal two-thirds	absent	blind sac

[a]Case 1 is from Greene et al. [1986].
[b]Case 2 is from Zuppan et al. [1986].
[c]NR, not reported.

the encephalocele. The sections also showed an additional, thin, noninfarcted neuroglial cyst wall adjacent to the cerebellar folia, so that the encephalocele appeared to contain a portion of the posterior occipital lobe as well. The neuroglial cyst did not have an ependymal lining. The encephalocele contents were not inflamed, infarcted, or hemorrhagic.

Cerebral cortex neuronal migration was nearly complete, with full-term neuronal migration, but polymicrogyria, in all lobes. A few residual nests of primary neurons were found in central frontal white matter. Large, gliotic germinal matrix sites were identified adjacent to the lateral ventricle. Several central white matter microinfarctions with petechial hemorrhages were found in the parietal and occipital lobes, with many macrophages present in the infarcted areas. There was little evidence of reactive gliosis.

RADIOGRAPHIC FINDINGS

A lacunar skull (lückenschädel) was present (Fig. 2). There was bilateral Sprengel deformity of the scapula. No block or hemivertebrae were evident on the radiographs. Severe right radial hypoplasia was apparent, with absence of the thumb (Fig. 3). The right hand also had 2 carpal ossification centers (accelerated maturation), not present on the left. Metacarpals and proximal, middle, and distal phalanges were all normal. There were 11 pairs of ribs, with posterior fusions of the 2nd, 3rd, and 4th ribs bilaterally. Thoracic and lumbar vertebrae were normal. Long bones had over-constriction of their midportions. The distal femur epiphyses were ossified, whereas the proximal tibial epiphyses were not, compatible with a gestational age of 35 ± 2 weeks. The feet were normal, except for accelerated maturation, indicated by the bilateral presence of ossification of either the cuboid or one of the cuneiform bones.

Fig. 2. Lateral, full body film showing lückenschädel (lacunar skull) and relatively normal spine and long bones.

Fig. 3. Film of the upper thorax and right upper extremity showing Sprengel deformity (more severe on the left than on the right), several posteriorly fused thoracic ribs, hypoplastic radius with secondary ulnar bowing, absent thumb, and two carpal centers (accelerated maturation).

DISCUSSION

Occipital encephaloceles are meningeal extrusions through midline defects in occipital bone, containing varying amounts of brain tissue and spinal fluid [Ingraham and Swan, 1943]. Encephaloceles form after neural tube closure, and the lesions seen at birth are due to cranial bone disproportion relative to the volume of the expanding brain [Emery and Kalhan, 1970;

Leong and Shaw, 1979]. The incidence is roughly 1 per 3,000 births [Lorber, 1967; Adetiloye et al., 1993].

MURCS association was originally recognized by analysis of cases of vaginal atresia associated with skeletal abnormalities [Duncan et al., 1979]. Some 50 cases have been reported [Willemsen, 1982; Colavita et al., 1986; Greene et al., 1986; Lo Iudice et al., 1986; Méndez et al., 1986, 1992; Zuppan et al., 1986; Vaidya et al., 1987; Esakowitz and Yates, 1988; Mahajan et al., 1992]. The frequency is roughly 1 per 50,000 females [Strübbe et al., 1992].

As a single case, the combination of occipital encephalocele and MURCS could be due to chance. However, 2 previous cases indicate that central nervous system malformations and MURCS can be associated (Table I). Greene et al. [1986] reported a college student with MURCS association and a 4 × 6 cm cerebellar cyst found at autopsy. Cortical heterotopia was present, and no skull defect was described. Zuppan et al. [1986] examined at autopsy a 4-day-old girl with MURCS and a thoracolumbar meningomyelocele. Arnold-Chiari malformation, hydrocephalus, and cervicothoracic syringomyelia were secondary to the tethered cord. Thus, the precedent exists for neural tube anomalies in MURCS patients.

Paraxial mesoderm arises in the primitive streak embryo to form somites and intermediate mesoderm. Occipital, cervical, and thoracic somites occur in sequence, beginning around the 21st day [Hamilton and Mossman, 1972]. Occipital somites form the base of the skull, whereas cervical and thoracic somites form the neck and upper limbs. Intermediate mesoderm connected to cervical somites develops into the pronephros, which helps induce the mesonephros [Hamilton and Mossman, 1972]. The mesonephros in turn influences formation of the Müllerian ducts at the level of the 3rd thoracic somites [Gruenwald, 1941; O'Rahilly, 1977]. Thus, MURCS association has been ascribed to abnormal development of cervical and upper thoracic somites and the pronephros [Duncan et al., 1979].

Paraxial mesoderm precursors of occipital bone have been cited to explain defects of the occiput and neural tube, such as anencephaly and occipital encephaloceles [Leong and Shaw, 1979; Müller and O'Rahilly, 1991; Marín-Padilla, 1991]. Specifically, detailed analyses by Marín-Padilla [1991], p. 156, led to the conclusion that "primary paraxial mesodermal insufficiency affects formation of the axial basicranium and the elevation of the neural folds. The severity of the paraxial mesoderm insufficiency determines the degree of failure in closure of neural folds. In severe insufficiency, the neural folds fail to close altogether such that all components are affected (surface ectoderm, neural crest cells, supporting paraxial unsegmented and segmented mesoderm, and neuroectoderm)." Anencephaly may represent a severe defect in paraxial mesoderm, whereas occipital encephaloceles may represent a more moderate defect. Pathogenesis of spinal meningomyeloceles is thought to be similar [Leong and Shaw, 1979; Marín-Padilla, 1970, 1991].

This case supports the conclusion that neural tube defects may represent a part of MURCS association. From the embryology of encephaloceles and MURCS, we hypothesize that abnormal paraxial mesoderm affecting occipital, cervical, and thoracic somites and adjacent intermediate mesoderm may explain the anomalies observed.

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